

Remarks

Claims 18-23, 25, and 27-35 were pending in the subject application. By this Amendment, claims 18, 19, 25, and 27-29 have been amended and claim 22 has been cancelled. Support for the amendments to the claims can be found throughout the specification as originally filed, including at, for example, the text following Table 3E, and claims 5 and 22. No new matter has been added by these amendments. Accordingly, claims 18-21, 23, 25, and 27-35 are pending in the subject application and before the Examiner for consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 18-23, 25 and 27-35 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the claims now presented for examination.

Please note that the claims have been amended herein to further clarify the nature of the Y groups.

With regard to the legal test for meeting the requirements of 35 U.S.C. §112, second paragraph, the Court of Appeals for the Federal Circuit has stated:

The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, §112 demands no more. The degree of precision necessary for adequate claims is a function of the nature of the subject matter. *Miles Lab., Inc. v. Shandon, Inc.* 997 F.2d 870,875,27 USPQ2d 1123, 1126 (Fed. Cir. 1993) (internal citations omitted).

In the current case, the skilled artisan would have no difficulty in discerning the metes and bounds of the subject invention as now claimed. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claims 18-23, 25 and 27-35 have been rejected under 35 U.S.C. §112, first paragraph. The applicants respectfully traverse this ground for rejection because the applicants were in full possession of the claimed subject matter at the time of filing.

As noted above, the claims have been amended herein to further clarify the identity of the Y groups. As is evident from the applicants' disclosure, including the examples, Y is an amine group that provides the affinity ligand function for the claimed compounds. Note, for example, that all of the "Y" groups exemplified in the application are amines. Please also note the following text that immediately follows Table 3E:

Nature of amines (Y1, Y2 and Y3)

The amines selected from the synthesis of 3D libraries may be primary, secondary, aliphatic, aromatic, heterocyclic, aryl, chiral, charged or any combination of these.

Further, the examples make it quite clear that these amines are providing the affinity ligand function.

The test for an adequate written description has been stated in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. It is respectfully submitted that applicants have met this test given the teachings of the specification and the subject matter of the claims as amended herein.

Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 18-23, 25 and 27-35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Lowik *et al.* (WO 01/42228). The applicants respectfully traverse this ground for

rejection because the cited reference does not disclose or suggest the compounds of the claimed invention or their use.

Scheme I of the Lowik *et al.* reference illustrates a method for the synthesis of a macrocycle. The left column merely demonstrates that the triazine chain can be elongated before cyclisation. The linear triazine molecule itself is an intermediate for obtaining the macrocycle, and there is nothing to suggest that the linear triazine chain itself can act as an affinity ligand. This confirms that Lowik *et al.* believe that the macrocyclic feature is essential to its function. The intention of Lowik *et al.* is clearly to form larger 3-dimensional pockets that can form binding sites for the capture of small molecules, i.e. the exact opposite of the small affinity ligands of the subject invention.

In the only potentially relevant structures in the Lowik *et al.* reference, i.e. the immobilised compounds shown on Lowik's drawings sheet 7/8, the group corresponding to X in the current applicants' claims is a piperazine ring. Further, in the only compound that is to be used for separation purposes, i.e. compound 44 (as opposed to the earlier intermediates), there are three triazine rings and two or three groups corresponding to Y. The applicants' claims require that, if there are three triazine rings, there are four groups Y.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_\_ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

The functions of the compounds of Lowik *et al.* and those of the present invention are superficially similar but, in fact, quite different. The Lowik *et al.* compounds work by capturing the material of interest within the macrocyclic structure; the novel compounds of the current invention work by providing affinity ligands. Therefore, there would be no reason for the skilled artisan to modify the Lowik *et al.* compounds to arrive at the compounds of the current invention.

Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Lowik *et al.* reference.

Claims 18-23, 25 and 27-35 have also been rejected under 35 U.S.C. §103(a) as being unpatentable over Lowik *et al.* (WO 01/42228) and Atkinson *et al.* (GB 2 053,926). The applicants respectfully traverse this ground for rejection because the cited references, taken either alone or in combination, do not disclose or suggest the claimed subject matter.

The present invention addresses the problem of providing compounds and ligand libraries comprising two or more triazine groups with attached amine groups (Y), and to provide diversity and improved selectivity with respect to protein binding. The macrocyclic compounds of the prior art are not intended as affinity ligands (i.e. small ligand molecules that bind within a larger 3-dimensional binding site of the analyte). There is nothing in the prior art to suggest that macrocyclic ring compounds could be used as affinity ligands, as the intention was to form larger 3-dimensional pockets that would capture small molecules.

The Office Action states that Atkinson *et al.* disclose "various triazine compounds useful as affinity chromatography materials," but these do not include a sequence of triazine rings with attached amine Y groups that act as affinity ligands. Combining the references does not give this essential structural feature, i.e. that of affinity ligands, or its effect.

Thus, Atkinson *et al.* does not cure the aforementioned defects of the Lowik *et al.* reference. In particular, there is no suggestion of linking two or more triazine molecules together. By contrast, the presence of the triazine molecules in a specific dimensionality is key to the compounds of the present invention to act as an affinity ligand. It is the diversity created by the triazine framework that provides specific selectivity for certain molecules, and the ease with which that framework can be modified that allows its use for a large number of compounds with respect to protein binding. The molecules disclosed in Atkinson *et al* are far removed from the present invention.

An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant's disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Spinnable*, 56 CCPA 823, 160 USPQ 237, 243 (1969).

The macrocyclic ligand intermediates of Atkinson *et al* are not intended as affinity ligands, i.e. small ligand molecules that bind within a larger 3-dimensional binding site. There is nothing in the cited references, either taken alone or in combination, to suggest that macrocyclic ring precursors could be used as affinity ligands in their own right, as the intention was to form larger 3-dimensional pockets that would form affinity binding sites for the capture of small molecules.

Thus, one finds neither the suggestion nor the expectation of success in the cited references, either separately or combined. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103.

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

A handwritten signature in black ink that reads "David Saliwanchik". The signature is fluid and cursive, with a prominent dot over the 'i' in Saliwanchik.

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